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# GUEST COMMENTARY

## *qnr* Gene Nomenclature[▽]

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Since the plasmid-borne quinolone resistance gene *qnr* was reported in 1998 (8), many additional *qnr* alleles have been discovered on plasmids or the bacterial chromosome (reviewed in references 9 and 13). The plasmid-borne *qnr* genes currently comprise three families, *qnrA*, *qnrB*, and *qnrS*, differing from each other 40% or more in nucleotide sequence. Within each family, minor (≤10%) variation in sequence has defined a growing number of alleles. For the *qnrA* and *qnrS* families, the number of variants has been manageable, with general agreement on allele designations, but lately, the number of *qnrB* sequences submitted to GenBank has exploded, with the same *qnrB* allele number claimed for dissimilar sequences by different investigators and the same entry given new allele numbers from week to week.

To bring order into the current *qnrB* numbering chaos, we propose numbering the *qnr* alleles according to the following rules: (i) priority should be given first to published numbers, then to those in accepted or submitted manuscripts, and finally to the date of submission to GenBank; (ii) only full-length sequences should be assigned allele numbers; (iii) naturally occurring alleles, not those created by mutation, will be numbered; (iv) only nucleotide alterations that result in amino acid changes and not functionally silent substitutions should be taken into account; (v) one or more amino acid alterations define a new allele; (vi) variation in promoter sequences is not considered; (vii) demonstration that an allele in an established family causes reduced susceptibility to nalidixic acid or a fluoroquinolone is desirable but is not required; (viii) a new family (such as *qnrC*) should differ substantially from existing families (≥30% difference suggested in nucleotides or derived amino acids) and should be shown to affect quinolone susceptibility; (ix) a database of *qnr* allele designations will be maintained at http://www.lahey.org/qnrStudies; and (x) further allele numbers will be assigned upon application.

Another source of confusion is the presence of two potential in-frame initiation codons for some *qnrB* alleles. For other *qnrB* alleles, the first ATG is out of phase with the second. The

TABLE 1. Proposed Qnr allele designations

| Allele | GenBank accession number | | GenBank designation[a] | Reference or source |
|---|---|---|---|---|
| | Nucleotide | Protein | | |
| QnrA1 | AY070235 | AAL60061 | | 17 |
| QnrA2 | AY675584 | AAT79355 | | T. Li et al., unpublished |
| QnrA3 | DQ058661 | AAZ04782 | | 11 |
| QnrA4[b] | DQ058662 | AAZ04783 | | 11 |
| QnrA5[b] | DQ058663 | AAZ04784 | | 11 |
| QnrA6 | DQ151889 | AAZ78355 | | 2 |
| QnrB1 | DQ351241 | ABC86904 | | 6 |
| QnrB2 | DQ351242 | ABC86905 | | 6 |
| QnrB3 | DQ303920 | ABC17629 | | 14 |
| QnrB4 | DQ303921 | ABC17630 | | 14 |
| QnrB5 | DQ303919 | ABC17628 | | 4 |
| QnrB6 | EF520349 | ABP87778 | | X. Ma et al., unpublished |
| QnrB7 | EU043311 | ABW03156 | | 3 |
| QnrB8 | EU043312 | ABW03157 | | 3 |
| QnrB9 | EF526508 | ABP88094 | QnrB8 | M. Zhu et al., unpublished |
| QnrB10 | DQ631414 | ABG56269 | | 12 |
| QnrB11 | EF653270 | ABS30107 | QnrB9 | P. Rodriguez-Zulueta et al., unpublished |
| QnrB12 | AM774474 | CAO82104 | | 7 |
| QnrB13 | EU273755 | ABX72042 | QnrB12 | M. D. Tamang et al., unpublished |
| QnrB14 | EU273757 | ABX72044 | | M. D. Tamang et al., unpublished |
| QnrB15 | EU302865 | ABX72227 | | M. D. Tamang et al., unpublished |
| QnrB16 | EU136183 | ABV66096 | QnrB11 | J. Sanchez-Cespedes et al., unpublished |
| QnrB17 | AM919398 | CAP45902 | QnrB16 | J. Gonzalez-Lopez et al., unpublished |
| QnrB18 | AM919399 | CAP45903 | QnrB17 | J. Gonzalez-Lopez et al., unpublished |
| QnrB19 | EU432277 | ACA28712 | | V. Cattoir et al., unpublished |
| QnrS1 | AB187515 | BAD88776 | | 5 |
| QnrS2 | DQ485530 | ABF47470 | | 4 |
| QnrS3 | EU077611 | ABU52984 | | L. Yue et al., unpublished |

[a] Number currently in GenBank if different from that assigned.
[b] Known only in the chromosome of *Shewanella algae*.

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TABLE 2. Amino acid substitutions in QnrA1 to QnrA6

| Allele | Substitution at position: | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 39 | 54 | 108 | 116 | 127 | 130 | 161 | 213 |
| QnrA1 | Q | V | V | S | T | S | R | V |
| QnrA2 | R | | | A | A | | | I |
| QnrA3 | R | | I | | A | | | |
| QnrA4 | R | | I | | A | N | | |
| QnrA5 | R | | I | | A | | C | |
| QnrA6 | R | I | I | | A | | H | |

second ATG initiation codon, common to all, has been used here in numbering QnrB amino acids, and amino acid variations that would occur if the first initiation codon were used have been ignored. Consequently, QnrB proteins have 214 amino acids, whereas the QnrA and QnrS proteins are 218 amino acids in length.

*qnr* alleles in the GenBank database as of April 2008 were evaluated to identify unique sequences and then assigned allele numbers. Table 1 shows our proposed designations for *qnrA*, *qnrB*, and *qnrS*. No new full-length *qnrA* sequences were found, but a unique *qnrS* sequence was identified and designated *qnrS3*. Nineteen unique *qnrB* alleles were identified. GenBank listings for partial *qnrB* alleles (accession numbers EF421178, EF421180, EF571009, EF576718, EU127476, and EU325573) have been omitted. In addition, GenBank accession numbers EF634464 and EU093091 code for QnrB6, and accession number EU136182 encodes QnrB9. Accession number EU273765, expressed from the second potential start codon, is the same as QnrB13 in our listing. Tables 2, 3, and 4 show the amino acid alterations in particular variants. Although *qnrB* has the greatest number of sequence variants, amino acid differences are currently found at 27 of 214 possible sites (13%), a percentage less than the amino acid variability among TEM (20%) or SHV (27%) β-lactamases (http://www.lahey.org/Studies/).

*qnr* genes have also been found on the chromosomes of both gram-positive (15) and gram-negative bacteria. We propose that they be termed *qnr* from a particular organism or, where a shorter designation is needed, given distinguishing initials such as Efs*qnr* from *Enterococcus faecalis* (1), Pp*qnr* from *Photobacterium profundum* (10), Vp*qnr* from *Vibrio parahaemolyticus* (16), or Vv*qnr* from *Vibrio vulnificus* (10). *qnr* letter designations, such as *qnrA3* from *Shewanella algae* or Sa*qnrA3* should be used only if the gene is at least 70% identical to one of the established *qnr* families.


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TABLE 3. Amino acid substitutions in QnrB1 to QnrB19[a]

| Allele | Amino acid change at position: | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 11 | 18 | 20 | 21 | 22 | 55 | 60 | 79 | 80 | 94 | 129 | 142 | 144 | 151 | 162 | 163 | 168 | 171 | 186 | 188 | 198 | 202 | 204 | 205 | 212 | 213 | | | | |
| QnrB1 | A | D | E | I | E | N | N | M | S | S | A | V | I | A | F | S | T | A | F | I | G | N | S | L | M | V | I | | | | |
| QnrB2 | | N | | | | | | | A | | | | M | | | | | | | | R | | | | | I | | | | | |
| QnrB3 | | | | | | | K | | | | | | M | | | | | | | | | | | | | | | | | | |
| QnrB4 | T | | | V | | | | N | I | N | S | | M | T | | | S | | V | | | S | | | L | I | M | | | | |
| QnrB5 | T | | | V | | | | | V | | | | M | T | | | | | | | | S | | | | | | | | | |
| QnrB6 | | | | | | | | | A | | | | M | | | | | | | | | | | | | | | | | | |
| QnrB7 | | | | | | | | | A | | | | M | | | T | | | | | | | | | | I | | | | | |
| QnrB8 | T | | | V | | | | I | V | | | A | M | T | L | | S | T | | | | | A | | | I | | | | | |
| QnrB9 | | | | | | | | | A | | | | M | | | | | | | | | | | | | I | | | | | |
| QnrB10 | T | | | V | | | | | V | | | | M | T | | | | | | | | | | | | | | | | | |
| QnrB11 | T | | A | V | | | | I | V | | S | | M | T | | | S | | | V | | S | | I | L | | M | | | | |
| QnrB12 | T | | A | V | | | | I | V | | S | | M | T | | | S | | | V | | S | | I | L | | | | | | |
| QnrB13 | | | | | | | | | A | | | | M | | | | | | | | R | | | | | I | | | | | |
| QnrB14 | | | | | D | | | | A | | | | M | | | | | | | | | | | | T | I | | | | | |
| QnrB15 | | | | | | S | | | A | N | | | M | | | | | | | | | | | | | I | | | | | |
| QnrB16 | | | | | | | | | A | | | | M | T | | | | | | | | | | | | I | | | | | |
| QnrB17 | | | | | | | | | | | | | M | | | | | | | | | | | | | | | | | | |
| QnrB18 | | | | | D | | | | A | | | | M | | | | | | | | | | | | | | | | | | |
| QnrB19 | T | | | V | | | | | V | | | | M | T | | | | | | | | S | | | | | | | | | |

[a] Variations from the QnrB1 sequence numbered from the second potential ATG initiation codon are shown.

TABLE 4. Amino acid substitutions in QnrS1 to QnrS3

| Allele | Amino acid substitution at position: | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 5 | 11 | 12 | 16 | 21 | 31 | 41 | 44 | 89 | 91 | 102 | 106 | 120 | 148 | 201 | 206 | 207 | 216 |
| QnrS1 | N | H | N | K | L | S | T | V | F | A | T | H | S | N | A | L | I | Y |
| QnrS2 | R | | S | Q | I | C | A | I | L | E | A | N | T | H | S | Q | L | F |
| QnrS3 | | R | | | | | | | | | | | | | | | | |

## REFERENCES


1. **Arsène, S., and R. Leclercq.** 2007. Role of a *qnr*-like gene in the intrinsic resistance of *Enterococcus faecalis* to fluoroquinolones. Antimicrob. Agents Chemother. **51:**3254–3258.
2. **Cambau, E., C. Lascols, W. Sougakoff, C. Bebear, R. Bonnet, J. D. Cavallo, L. Gutmann, M. C. Ploy, V. Jarlier, C. J. Soussy, and J. Robert.** 2006. Occurrence of *qnrA*-positive clinical isolates in French teaching hospitals during 2002–2005. Clin. Microbiol. Infect. **12:**1013–1020.
3. **Cattoir, V., L. Poirel, V. Rotimi, C. J. Soussy, and P. Nordmann.** 2007. Multiplex PCR for detection of plasmid-mediated quinolone resistance *qnr* genes in ESBL-producing enterobacterial isolates. J. Antimicrob. Chemother. **60:**394–397.
4. **Gay, K., A. Robicsek, J. Strahilevitz, C. H. Park, G. Jacoby, T. J. Barrett, F. Medalla, T. M. Chiller, and D. C. Hooper.** 2006. Plasmid-mediated quinolone resistance in non-Typhi serotypes of *Salmonella enterica*. Clin. Infect. Dis. **43:**297–304.
5. **Hata, M., M. Suzuki, M. Matsumoto, M. Takahashi, K. Sato, S. Ibe, and K. Sakae.** 2005. Cloning of a novel gene for quinolone resistance from a transferable plasmid in *Shigella flexneri* 2b. Antimicrob. Agents Chemother. **49:** 801–803.
6. **Jacoby, G. A., K. E. Walsh, D. M. Mills, V. J. Walker, H. Oh, A. Robicsek, and D. C. Hooper.** 2006. *qnrB*, another plasmid-mediated gene for quinolone resistance. Antimicrob. Agents Chemother. **50:**1178–1182.
7. **Kehrenberg, C., S. Friederichs, A. de Jong, and S. Schwarz.** 2008. Novel variant of the *qnrB* gene, *qnrB12*, in *Citrobacter werkmanii*. Antimicrob. Agents Chemother. **52:**1206–1207.
8. **Martínez-Martínez, L., A. Pascual, and G. A. Jacoby.** 1998. Quinolone resistance from a transferable plasmid. Lancet **351:**797–799.
9. **Nordmann, P., and L. Poirel.** 2005. Emergence of plasmid-mediated resistance to quinolones in Enterobacteriaceae. J. Antimicrob. Chemother. **56:** 463–469.
10. **Poirel, L., A. Liard, J. M. Rodriguez-Martinez, and P. Nordmann.** 2005. Vibrionaceae as a possible source of Qnr-like quinolone resistance determinants. J. Antimicrob. Chemother. **56:**1118–1121.
11. **Poirel, L., J. M. Rodriguez-Martinez, H. Mammeri, A. Liard, and P. Nordmann.** 2005. Origin of plasmid-mediated quinolone resistance determinant QnrA. Antimicrob. Agents Chemother. **49:**3523–3525.
12. **Quiroga, M. P., P. Andres, A. Petroni, A. J. Soler Bistué, L. Guerriero, L. J. Vargas, A. Zorreguieta, M. Tokumoto, C. Quiroga, M. E. Tolmasky, M. Galas, and D. Centrón.** 2007. Complex class 1 integrons with diverse variable regions, including *aac(6′)-Ib-cr*, and a novel allele, *qnrB10*, associated with IS*CR1* in clinical enterobacterial isolates from Argentina. Antimicrob. Agents Chemother. **51:**4466–4470.
13. **Robicsek, A., G. A. Jacoby, and D. C. Hooper.** 2006. The worldwide emergence of plasmid-mediated quinolone resistance. Lancet Infect. Dis. **6:**629–640.
14. **Robicsek, A., J. Strahilevitz, D. F. Sahm, G. A. Jacoby, and D. C. Hooper.** 2006. *qnr* prevalence in ceftazidime-resistant *Enterobacteriaceae* isolates from the United States. Antimicrob. Agents Chemother. **50:**2872–2874.
15. **Rodríguez-Martínez, J. M., C. Velasco, A. Briales, I. García, M. C. Conejo, and A. Pascual.** 2008. Qnr-like pentapeptide repeat proteins in gram-positive bacteria. J. Antimicrob. Chemother. **61:**1240–1243.
16. **Saga, T., M. Kaku, Y. Onodera, S. Yamachika, K. Sato, and H. Takase.** 2005. *Vibrio parahaemolyticus* chromosomal *qnr* homologue VPA0095: demonstration by transformation with a mutated gene of its potential to reduce quinolone susceptibility in *Escherichia coli*. Antimicrob. Agents Chemother. **49:** 2144–2145.
17. **Tran, J. H., and G. A. Jacoby.** 2002. Mechanism of plasmid-mediated quinolone resistance. Proc. Natl. Acad. Sci. USA **99:**5638–5642.


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